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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,823	06/26/2001	John R. Neefe	12071-003001	2643

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EXAMINER	
SALIMI, ALI REZA	

ART UNIT	PAPER NUMBER
1648	18

DATE MAILED: 04/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/891,823	Applicant(s) Neefe et al
	Examiner A. R. SALMI	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 15, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 6, 8-13, and 36-80* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6, 8-13, and 36-80* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). 14
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

This is a response to the amendment B, paper No.17, filed 4/15/2003. Claims 5, 7, 14-35 have been canceled. Claims 36-80 have been added. Claims 1-4, 6, 8-13, and 36-80 are pending before the examiner.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Please note any grounds of rejection that has not been repeated is removed.

Claim Rejections - 35 USC § 112

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 112, second paragraph, for reasons of record advanced in the previous Office Action mailed 10/16/2002. Applicant argues that "immunostimulatory fragment" and "antigenic fragment" in view of the specification and the skilled in the art has clear meaning. In addition, with regard to "sufficient amount" applicants argue that the amount may vary depending on the subject. Applicant's argument as part of amendment B, Paper NO. 17, filed 4/15/2003 has been considered fully, but they are not persuasive. At the onset applicant are reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Since the specification does not set forth the intended metes and bounds of the "immunostimulatory fragment" and "antigenic

fragment"which can be utilized in the method, the claims are vague and indefinite. The mere recitation of a so called functional language does not take away from the indefiniteness of the claims. When one of skilled in the art looks to see what the "antigenic fragments" or "immunostimulatory fragment" can be, and finds none, that would amount to the lack of clarity and as a consequence the claims are indefinite. In addition, with regard to "sufficient amount", the claim 1 should provide at least a range of what considers to be "sufficient" amount. The office did not ask for an amount that can apply to only a man weighing 170 lbs, the sufficient amount that can be used in the method so to provide clarity is required so the wart can be "sufficiently treated". The rejection is maintained.

Claim Rejections - 35 USC § 112

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced in the previous Office Action mailed 10/16/2002. Applicants argue that the claims are now directed to "HPV E7", and "HsP60", and HsP60 being a family of proteins that includes HsP65, hence, the term is properly used to describe the family to which the mycobacterial HsP65 belong. Additionally, applicants argue that fragments and "immunostimulatory fragment defined by their function can be easily made given the level of skill in the art and can e employed in the method. Applicant's argument as part of amendment B, Paper NO. 17, filed 4/15/2003 has been considered fully, but they are not persuasive. Applicants do not address the deficient teaching of the specification that would force one of ordinary skill in

the art into undue experimentation to enable the broad scope of the claimed invention as it was articulated by the Office in previous action. They do not address why they should be entitled to a "family" of immunostimulatory molecules, if its so routine and simple then why applicants have only observed full length HsP65 fused to full length HPV-16 E7 protein? Extrapolation from one fusion cannot be translated for any and all whole host of molecules. Absent adequate teaching one of ordinary kill would be forced into extensive undue experimentation to enable the full scope of the claimed invention. Applicants are asking others to enable their claimed invention. Applicants are the ones requesting patent protection and for that exclusive protection they should provide adequate teaching. Applicants are dismissing the concerned raised as merely routine, but such is not the case since Applicants own disclosure states that this field is highly unpredictable and yet applicants now make assertions that everything is routine, this has to be reconciled (emphasis added). The specification does not teach how a "wart" can be treated with a "sufficient amount" of a fragment of any human papillomavirus E7, fused with a fragment of HsP60, or any other "family" of stress proteins, which the fusion protein is suppose to treat a wart infected with a different type of HPV than the employed epitopic fragment HPV used in the fusion protein. There has to be overlapping regions between the HPV E7 region used in the fusion protein and the wart infected with a "different" papillomavirus, otherwise no "sufficient treatment" is going to take place (emphasis added). Applicants have "observed" (emphasis added) that fusion of the entire E7 protein and entire HsP65 will induce immune response to reduce the wart size. There are no teaching in the specification that would merit the broad protection that applicants are seeking,

absent undue experimentation. The whole host of epitopes and fragments of HsP60 or even HsP65 would not induce the desired response, just because there is so called functional language present doe not take away form the fact that undue experimentation would be required to enable the full scope of the claimed invention. Moreover, there is no teaching as to whether or not the fragment of heat shock would be a proper chaperoned to the peptide. There is no teaching whether or not the auto-immune response would not result, which absent teaching undue experimentation would be required to practice the invention. The rejection is respectfully maintained.

Claim Rejections - 35 USC § 112

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention, for reasons of record advanced in the previous Office Action mailed 10/16/2002. Applicants argue that since the HsP60 fragments is limited both by structure as well as function then the written description requirements is satisfied. Applicant's argument as part of amendment B, Paper NO. 17, filed 4/15/2003 has been considered fully, but they are not persuasive. Applicants are on the record stating that HsP60 belongs to a family of proteins which includes HsP65, see top of page 9 of the paper no. 17. The specification does not set forth the metes and bounds of multiple myriads of complexed proteins

which can be employed in a method, there is not enough information about it in literature either to guide the one of ordinary skill in the art to predict the undisclosed regions where the region may encompass, and/or predict the complex of any and all epitope with any and all HsP60 protein permutation. There is nothing in the specification that indicates applicants have taught or possessed the structures of the "fragments" of either "immunostimulatory fragment" or the "HPV E7" protein. Defining something by its "functional capability" is not the same as possession of that thing, this amounts to fishing exhibition and not full filing the written description. There is nothing in the disclosure that shows applicants have taught any fragment structure of the family of HsP60. Therefore, since applicants were not in possession of material that can be used in a method, as a consequence the written description of invention is lacking. The rejection is maintained.

Claim Rejections - 35 USC § 102

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Mizzen et al (WO 99/07860),for reasons of record advanced in the previous Office Action mailed 10/16/2002. Applicants argue that Mizzen's disclosure does not anticipate independent claim 1, because Mizzen does not describe using a fusion protein containing an HPV protein antigen of one HPV type to treat wart caused by an infection with a second HPV type. Applicants conclude, accordingly Mizzen cannot anticipate the claimed invention. Applicant's argument as part of amendment B, Paper NO. 17, filed 4/15/2003 has been considered fully, but they are not persuasive. The question that should be asked and answered is whether or not the

composition and methods taught by Mizzen et al in the above cited reference would anticipate the claimed invention or not. The answer is clearly, Yes (emphasis added). The facts are the fusion taught and claimed by Mizzen et al once administered by the method taught by Mizzen et al would inherently "reduce" or "treat" the "wart", since the wart which is caused by a human papillomavirus type would have overlapping epitopic region which Mizzen's fusion protein upon induction of immune response would also manage to treat. The Office's position is that the fusion of Mizzen would inherently treat the second papillomavirus which has infected the wart. Applicants have not provided any evidence to the contrary. In addition, the "fragment" recitation is also anticipated by the disclosure of the above cited art. Moreover, applicants are directed to **In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CA FC 2002)**, wherein the Federal Circuit cited authority for the rule that, "a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." The court said, "While Brassica may have recognized something quite interesting about those sprouts, it simply has not invented anything new." This is the case here, while the Applicants may have "Observed" something interesting they have not have anything new. The rejection is maintained.

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chu et al (FASEB Journal, March 20, 1998, 12 (5): A909), for reasons of record advanced in the previous Office Action mailed 10/16/2002. Applicants argue that because Chu does not describe using a fusion protein containing an HPV protein antigen of one HPV type to

treat wart caused by an infection with a second HPV type. Applicants conclude, accordingly Chu cannot anticipate the claimed invention. Applicant's argument as part of amendment B, Paper NO. 17, filed 4/15/2003 has been considered fully, but they are not persuasive. Chu et al would inherently "reduce" or "treat" the "wart", since the wart which is caused by a human papillomavirus type would have overlapping epitopic region which Chu's fusion protein upon induction of immune response would also manage to treat. The Office's position is that the fusion of Chu et al would inherently treat the second papillomavirus which has infected the wart. Applicants have not provided any evidence to the contrary. In addition, the "fragment" recitation is also anticipated by the disclosure of the above cited art. Moreover, applicants are directed to In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CA FC 2002)wherein the Federal Circuit cited that, "a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." The court said, "While Brassica may have recognized something quite interesting about those sprouts, it simply has not invented anything new." This is the case here, while the Applicants may have "Observed" something interesting they have not have anything new. The rejection is maintained.

Claim Rejections - 35 USC § 102

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Zhou G (Chinese Patent No. CN1248631A, March 2000), for reasons of record advanced in the previous Office Action mailed 10/16/2002. Applicants argue that because Zhou

does not describe using a fusion protein containing an HPV protein antigen of one HPV type to treat wart caused by an infection with a second HPV type, Applicants conclude, accordingly Zhou cannot anticipate the claimed invention. Applicant's argument as part of amendment B, Paper NO. 17, filed 4/15/2003 has been considered fully, but they are not persuasive. Zhou would inherently "reduce" or "treat" the "wart", since the wart which is caused by a human papillomavirus type would have overlapping epitopic region which Zhou's fusion protein upon induction of immune response would also manage to treat (see claims at least claims 1-4). The Office's position is that the fusion of Zhou's would inherently treat the second papillomavirus which has infected the wart. Applicants have not provided any evidence to the contrary. In addition, the "fragment" recitation is also anticipated by the disclosure of the above cited art. Moreover, applicants are directed to In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CA FC 2002)wherein the Federal Circuit cited that, "a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." The court said, "While Brassica may have recognized something quite interesting about those sprouts, it simply has not invented anything new." This is the case here, while the Applicants may have "Observed" something interesting they have not have anything new. The rejection is maintained.

NEW GROUNDS OF REJECTION:

Claim Rejections - 35 USC § 112

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite for recitation of "HsP60" is this a trademark or a made-up acronym? The intended metes and bounds of "HsP60" is not defined. Is this chaperon protein isolated form a human tumor or is this bacterial protein. In addition, the intended metes and bounds of the "immunostimulatory fragment thereof" is not defined. In addition, the fragment of E7 protein is not defined. The claim has been interpreted in light of the specification, and since the specification does not provide a concise teaching one is not appraised of it scope and/or intended boundaries. This affects the dependent claims.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the "immunostimulatory fragment" which would be suited to treat HPV, the HPV E7 protein and its "fragment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 102(e) as being anticipated by Mizzen et al (U.S Patent No. 6,524,825 B1).

The teaching and the claims of the above cited patent clearly anticipates the claimed invention (for instance see claims 1, 2, 4, 9-11, 25, 26, 27, 58, and 59). The Office's position is that the fusion of Mizzen et al would inherently treat the second papillomavirus which has infected the wart. Applicants have not provided any evidence to the contrary. Regarding the modification of using composition titters within the broad recited range is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995) because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233. Moreover, applicants are directed to In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CA FC 2002),

wherein the Federal Circuit cited authority for the rule that, "a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." The court said, "While Brassica may have recognized something quite interesting about those sprouts, it simply has not invented anything new." This is the case here, while the Applicants may have "Observed" something interesting they have not have anything new.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1-4, 6, 8-13, and 36-80 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Applicants' specification states during a clinical trial for determining the efficacy of fusion polypeptide of human papilloma virus (HPV) E7 protein coupled to M. Bovis BCG HsP65 which is member of HsP60 family was provided to the applicants by the inventors listed in the reference WO 99/07860 (for instance see page 18 of the specification). During conducting the clinical trial applicants came way with an observation (emphasis added) that the composition and method taught by the inventors of WO 99/07860 also reduces "anogenital warts" wherein the warts are also infected with HPV. Clearly multiple HPVs

share antigenic regions, so it is not surprising to see that as a secondary target the product of the above cited reference would also treat the wart that shares the same antigenic region as the primary target. However, this is an observation, but Applicants have not invented anything. To further substantiate the above assertions applicants are directed to Goldstone et al , 2002, Dis. Colon Rectum, 45:502-507, see IDS AE of paper no. 5. Goldstone et al reports that the results are from a clinical trial sponsored by Stressgen wherein HsPE7, specifically entire bacterial HsP65 where fused to full length HPV-16 E7 and was given to the authors by Stressgen, wherein they admit the results were tabulated from a retrospective review of the medical records, and prospective measurement were not taken (see page 506, left column, 2nd full paragraph, and page 506 right column, 3rd paragraph). This further substantiates the Office's position that Applicants are not inventors, rather the true inventors are the ones named in the WO 99/07860.

No Claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to A. R. Salimi whose telephone number is (703) 305-7136. The examiner can normally be reached on Monday-Friday from 9:00 Am to 6:00 Pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-3014, or (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

A. R. Salimi

4/25/2003

ALI R. SALIMI
PRIMARY EXAMINER